

Please insert new claims 22-81, as follows:

22. (New) A solid pharmaceutical dosage form adapted for direct oral administration across the oral mucosa comprising:

Sub  
a pharmaceutically effective amount of an orally administerable medicament; and  
at least one saliva activated effervescent agent present in an amount between about 5% by weight and 80% by weight.

23. (New) The solid pharmaceutical dosage form of claim 22, wherein said effervescent agent is present in an amount between about 20% by weight and 80% by weight.

24. (New) The solid pharmaceutical dosage form of claim 22, further comprising at least one pH adjusting substance.

25. (New) The solid pharmaceutical dosage form of claim 22, further comprising a bioadhesive, wherein said bioadhesive increases the contact time between said dosage form and the oral mucosa.

26. (New) The solid pharmaceutical dosage form of claim 22, further comprising a non-effervescent disintegration agent.

27. (New) The solid pharmaceutical dosage form of claim 22, further comprising glidants, lubricants, binders, sweeteners, flavoring and coloring components.

28. (New) The solid pharmaceutical dosage form of claim 22, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihypertensives, tranquilizers, decongestants, and beta blockers.

29. (New) The solid pharmaceutical dosage form of claim 22, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

30. (New) A solid pharmaceutical dosage form adapted for direct oral administration across the oral mucosa comprising:

Sub  
cont.  
a pharmaceutically effective amount of an orally administerable medicament; at least one saliva activated effervescent agent present in an amount sufficient to increase absorption of said orally administerable medicament across the oral mucosa; and

• one or more glidants, lubricants, binders, sweeteners, flavoring, non-effervescent disintegration agents or coloring components.

31. (New) The solid pharmaceutical dosage form of claim 30, further comprising at least one pH adjusting substance.

32. (New) The solid pharmaceutical dosage form of claim 30, further comprising a bioadhesive, wherein said bioadhesive increases the contact time between said dosage form and the oral mucosa.

33. (New) The solid pharmaceutical dosage form of claim 30, comprising a non-effervescent disintegration agent selected from the group consisting of microcrystalline cellulose, croscarmellose sodium, crospovidone, corn starch, potato starch, modified corn starch, modified potato starch, bentonite, alginates, agar, guar, locust bean, karaya, pectin and tragacanth..

34. (New) The solid pharmaceutical dosage form of claim 30, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, and beta blockers.

35. (New) The solid pharmaceutical dosage form of claim 30, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

36. (New) The solid pharmaceutical dosage form of claim 30, wherein said at least one saliva activated effervescent agent is present in an amount between about 20% by weight and 80% by weight.

37. (New) A method of administering at least one systemically distributable pharmaceutical agent across the oral mucosa comprising:

- a) providing a solid oral dosage form including
  - i. a pharmaceutically effective amount of an orally administerable medicament,
  - ii. at least one effervescent agent in an amount sufficient to increase absorption of said orally administrable medicament across the oral mucosa, and
  - iii. a pH adjusting substance in amount additional to the amount required for effervescence, said amount being tolerable to the subject, wherein said pH adjusting substance and said amount thereof are selected to alter pH of a local environment of said medicament to control the relative concentrations of ionized and unionized forms of said medicament; and
- b) placing said solid oral dosage form in the mouth of a patient so that saliva in said patient's mouth activates said at least one effervescent agent in said tablet; and
- c) holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in the mouth of a patient wherein said at least one effervescent agent promotes absorption of said orally administerable medicament across the oral mucosa.

38. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said step c) includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth adjacent a cheek for buccal administration.

39. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said step c) includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth beneath the tongue for sublingual administration.

40. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said step c) includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth between the upper lip and gum for gingival administration.

BA  
cont.  
41. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said solid oral dosage form further includes a bioadhesive, wherein said bioadhesive increases the contact time between said solid oral dosage form and the oral mucosa.

42. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said solid oral dosage form further includes glidants, lubricants, binders, sweeteners, flavoring and coloring components.

43. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, and beta blockers.

44. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

45. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said at least one effervescent agent is present in an amount between about 5% by weight and 95% by weight.

46. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said at least one effervescent agent is present in an amount between about 20% by weight and 80% by weight.

47. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said at least one effervescent agent is present in an amount sufficient to evolve a gas in an amount between about 5 cm<sup>3</sup> to about 30 cm<sup>3</sup>.

48. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said pH adjusting substance and said amount thereof are selected to favor the ionized form of said medicament.

49. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said pH adjusting substance and said amount thereof are selected to favor the unionized form of said medicament.

50. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said pH adjusting substance is a base.

51. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said base is selected from the group consisting of sodium carbonate, potassium carbonate, magnesium carbonate, disodium hydrogen phosphate, sodium dihydrogen phosphate, dipotassium hydrogen phosphate, and potassium dihydrogen phosphate.

52. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 17, wherein said non-effervescent disintegration agent is

selected from the group consisting of microcrystalline cellulose, croscarmellose sodium, crospovidone, corn starch, potato starch, modified corn starch, modified potato starch, bentonite, alginates, agar, guar, locust bean, karaya, pectin and tragacanth.

Rule  
1.126

~~53. 52. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said medicament is prochlorperazine.~~

~~54. 53. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 37, wherein said amount of said effervescent agent in said dosage form is selected to produce between about 5 cm<sup>3</sup> and about 30 cm<sup>3</sup> of evolved gas upon exposure to an aqueous environment.~~

~~55. 54. (New) A method of administering at least one systemically distributable pharmaceutical agent across the oral mucosa comprising:~~

- ~~a. providing a solid oral dosage form including~~
- ~~i. a pharmaceutically effective amount of an orally administerable medicament, and~~
- ~~ii. at least one effervescent agent present in the amount between about 5% by weight and about 80% by weight;~~

~~b. placing said solid oral dosage form in the mouth of a patient so that saliva in said patient's mouth activates said at least one effervescent agent in said tablet; and~~

~~c. holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in the mouth of a patient wherein said at least one effervescent agent promotes absorption of said orally administerable medicament across the oral mucosa.~~

~~56. 55. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said step c. includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth adjacent a cheek for buccal administration.~~

Re  
Cont.

57.

56. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said step c. includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth beneath the tongue for sublingual administration.

58.

57. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said step c. includes holding said solid oral dosage form and the dissolving contents of said solid oral dosage form in said mouth between the upper lip and gum for gingival administration.

59.

58. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said solid oral dosage form further includes a bioadhesive, wherein said bioadhesive increases the contact time between said solid oral dosage form and the oral mucosa.

60.

59. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said solid oral dosage form further includes glidants, lubricants, binders, sweeteners, flavoring and coloring components.

61.

60. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, and beta blockers.

62.

61. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

63.

62. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said at least one effervescent agent is present in an amount between about 20% by weight and 80% by weight.

64.

63. (New) The method of administering at least one systemically distributable pharmaceutical agent according to claim 54, wherein said at least one effervescent agent is present in an amount sufficient to evolve a gas in an amount between about 5 cm<sup>3</sup> to about 30 cm<sup>3</sup>.

65.

64. (New) A method of manufacturing a solid pharmaceutical dosage form suitable for direct oral administration across the oral mucosa, said method comprising

a) mixing a pharmaceutically effective amount of an orally administrable medicament, at least one saliva-activated effervescent agent present in an amount from about 5% by weight to about 80% by weight, and at least one pH adjusting substance in amount additional to the amount required for effervescence; and

b) using said mixture to produce said solid pharmaceutical dosage form.

66.

65. (New) The method of claim 64, wherein said solid pharmaceutical dosage further comprises at least one bioadhesive.

67.

66. (New) The method of claim 64, wherein said solid pharmaceutical dosage further comprises a non-effervescent disintegration agent.

68.

67. (New) The method of claim 64, wherein said solid pharmaceutical dosage further comprises one or more glidants, lubricants, binders, sweeteners, flavoring and coloring components.

69.

68. (New) The method of claim 64, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics,



antiflatuents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, and beta blockers.

~~70. (New) The method of claim 64, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.~~

~~71. (New) The method of claim 64, wherein said at least one saliva activated effervescent agent is present in an amount between about 20% by weight and 80% by weight.~~

~~72. (New) A method of manufacturing a solid pharmaceutical dosage form suitable for direct oral administration across the oral mucosa, said method comprising~~

- ~~a) mixing~~
- ~~i. a pharmaceutically effective amount of an orally administerable medicament,~~
- ~~ii. at least one effervescent agent in an amount sufficient to increase absorption of said orally administrable medicament across the oral mucosa, and~~
- ~~iii. a pH adjusting substance in amount additional to the amount required for effervescence, said amount being tolerable to the subject, wherein said pH adjusting substance and said amount thereof are selected to alter pH of a local environment of said medicament to control the relative concentrations of ionized and unionized forms of said medicament; and~~
- ~~b) using said mixture to produce said solid pharmaceutical dosage form.~~

~~73. (New) The method according to claim 71, wherein said solid oral dosage form further includes glidants, lubricants, binders, sweeteners, flavoring and coloring components.~~

~~74. (New) The method according to claim 71, wherein said orally administerable medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines,~~

antiasthmatics, antidiuretics, antiflatuents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, and beta blockers.

75.

74. (New) The method according to claim 71, wherein said orally administerable medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

76.

75. (New) The method according to claim 71, wherein said at least one effervescent agent is present in an amount between about 5% by weight and 95% by weight.

77.

76. (New) The method according to claim 71, wherein said at least one effervescent agent is present in an amount between about 20% by weight and 80% by weight.

78.

77. (New) The method according to claim 71, wherein said at least one effervescent agent is present in an amount sufficient to evolve a gas in an amount between about 5 cm<sup>3</sup> to about 30 cm<sup>3</sup>.

79.

78. (New) The method according to claim 71, wherein said pH adjusting substance and said amount thereof are selected to favor the ionized form of said medicament.

80.

79. (New) The method according to claim 71, wherein said pH adjusting substance and said amount thereof are selected to favor the unionized form of said medicament.

81.

80. (New) The method according to claim 71, wherein said pH adjusting substance is a base.

82.

81. (New) The method according to claim 71, wherein said base is selected from the group consisting of sodium carbonate, potassium carbonate, magnesium carbonate, disodium hydrogen phosphate, sodium dihydrogen phosphate, dipotassium hydrogen phosphate, and potassium dihydrogen phosphate.